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|-------------------------------|------------------------|---------------------|--|
| <b>Notice of Allowability</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                               | 10/824,027             | EYK ET AL.          |  |
|                               | Examiner               | Art Unit            |  |
|                               | Anand U. Desai, Ph.D.  | 1656                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTO-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1.  This communication is responsive to November 3, 2006.
2.  The allowed claim(s) is/are 16, 17, 19 and 21-37.
3.  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a)  All
  - b)  Some\*
  - c)  None
  1.  Certified copies of the priority documents have been received.
  2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3.  Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4.  A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5.  CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a)  including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1)  hereto or 2)  to Paper No./Mail Date \_\_\_\_\_.
  - (b)  including changes required by the attached Examiner's Amendment / Comment or in the Office action of
    - Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6.  DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

#### Attachment(s)

1.  Notice of References Cited (PTO-892)
2.  Notice of Draftsperson's Patent Drawing Review (PTO-948)
3.  Information Disclosure Statements (PTO/SB/08),  
Paper No./Mail Date 20061103
4.  Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5.  Notice of Informal Patent Application
6.  Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_.
7.  Examiner's Amendment/Comment
8.  Examiner's Statement of Reasons for Allowance
9.  Other \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 3, 2006 has been entered.

### ***Information Disclosure Statement***

2. The information disclosure statement (IDS) submitted on November 3, 2006 is being considered by the examiner.

## **EXAMINER'S AMENDMENT**

3. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Dr. Kathleen Tyrrell on December 15, 2006.

Examiner's amendment to the claims:

16. (Currently Amended) A method for identifying an agent capable of priming which primes a cell for preconditioning and/or inducing preconditioning of a cell, tissue, or organ comprising:

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a) obtaining a cell, tissue, or organ that comprises an endogenous preconditioning protein, selected from the group consisting of isocitrate dehydrogenase NAD<sup>+</sup> specific subunit alpha, succinyl CoA ligase, 23 kDa mitochondrial precursor subunit of Complex I, 24 kDa mitochondrial precursor subunit of Complex I, 30 kDa mitochondrial precursor subunit of Complex I, δ chain of the F<sub>1</sub> portion of Complex V, d chain of the F<sub>0</sub> portion of Complex V, prohibitin, ADP ribosyl hydrolase, HSP27 and RNA binding protein regulatory subunit (DJ-1);

b) providing the agent to said cell, tissue, or organ; assessing the ability of the agent to increase abundance of a preconditioning protein in a cell, tissue or organ by

c) detecting an increase in abundance of the preconditioning protein in the presence of the agent as compared to the abundance of preconditioning protein in the absence of the agent[[,]]; and thereby wherein the agent identified increases the abundance of one or more preconditioning proteins selected from the group consisting of isocitrate dehydrogenase NAD<sup>+</sup> specific subunit alpha, succinyl CoA ligase, a 23 kDa mitochondrial precursor subunit of Complex I, a 24 kDa mitochondrial precursor subunit of Complex I, a 30 kDa mitochondrial precursor subunit of Complex I, a δ chain mitochondrial precursor of the F<sub>1</sub> portion of Complex V, a d chain mitochondrial precursor of the F<sub>0</sub> portion of Complex V, prohibitin, ADP ribosyl hydrolase, HSP27 and RNA binding protein regulatory subunit (DJ-1)

d) identifying an agent that primes a cell for preconditioning and/or inducing preconditioning of a cell, tissue, or organ.

17. (Currently Amended) A method for identifying an agent which primes a cell for preconditioning and/or inducing preconditioning of a cell, tissue, or organ comprising:

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a) obtaining a cell, tissue, or organ that comprises an endogenous preconditioning protein, selected from the group consisting of dihydrolipoamide succinyltransferase, core protein I of Complex III, metaxin 2 and sarcalumein;

b) providing the agent to said cell, tissue, or organ;

c) detecting a decrease in abundance of the preconditioning protein in the presence of the agent as compared to the abundance of preconditioning protein in the absence of the agent; and thereby

d) identifying an agent that primes a cell for preconditioning and/or inducing preconditioning of a cell, tissue, or organ.

A method for identifying an agent capable of priming a cell for preconditioning and/or inducing preconditioning of a cell, tissue or organ comprising assessing the ability of the agent to decrease abundance of a preconditioning protein in a cell, tissue, or organ by detecting a decrease in abundance of the preconditioning protein in the presence of the agent as compared to the abundance of preconditioning protein in the absence of the agent, wherein the agent identified decreases the abundance of one or more preconditioning proteins selected from the group consisting of dihydrolipoamide succinyltransferase, core protein I of Complex III, metaxin 2 and sarcalumein.

18. (Cancelled).

19. (Currently Amended) A method for identifying an agent which primes a cell for preconditioning and/or inducing preconditioning of a cell, tissue, or organ comprising:

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- a) obtaining a cell, tissue, or organ that comprises an endogenous preconditioning protein, selected from the group consisting of the β chain of the F<sub>1</sub> portion of Complex V or protein X;
- b) providing the agent to said cell, tissue, or organ;
- c) detecting an increase in post-translational modification of the preconditioning protein in the presence of the agent as compared to the post-translational modification of the preconditioning protein in the absence of the agent; and thereby
- d) identifying an agent that primes a cell for preconditioning and/or inducing preconditioning of a cell, tissue, or organ.

~~A method for identifying an agent capable of priming a cell for preconditioning and/or inducing preconditioning of a cell, tissue or organ comprising assessing the ability of the agent to increase post translational modification of β chain mitochondrial precursor of the F<sub>1</sub> portion of Complex V or protein X in a cell, tissue or organ by detecting an increase in post translational modification of β chain mitochondrial precursor of the F<sub>1</sub> portion of Complex V or protein X in the presence of the agent as compared to the post translational modification of β chain mitochondrial precursor of the F<sub>1</sub> portion of Complex V or protein X in the absence of the agent.~~

26. (Currently Amended) The method of claim 16 wherein the preconditioning protein is the δ chain ~~mitochondrial precursor~~ of the F<sub>1</sub> portion of Complex V.

27. (Currently Amended) The method of claim 16 wherein the preconditioning protein is the d chain ~~mitochondrial precursor~~ of the F<sub>0</sub> portion of Complex V.

36. (Currently Amended) The method of claim 19 wherein the agent increases post-translational modification of the β chain ~~mitochondrial precursor of~~ the F<sub>1</sub> portion of Complex V.

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***Allowable Subject Matter***

4. Claims 16, 17, 19, and 21-37 are allowable.
5. The following is an examiner's statement of reasons for allowance: The prior art does not disclose the Markush proteins conferring the preconditioning process to a cell. The prior art does not disclose a method of identifying an agent capable of priming a cell for preconditioning and/or inducing preconditioning by detecting an increase or decrease in the abundance of the respective preconditioning proteins recited in the Markush groups.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

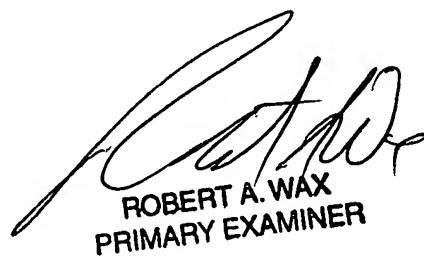
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

December 15, 2006



ROBERT A. WAX  
PRIMARY EXAMINER